

REMARKS

The pending claims are claims 1-21, 31-38, 40-48, and 53-64.

Request for Continued Examination

Applicant hereby requests a Request for Continued Examination under 37 C.F.R. §1.114.

Submission of Supplemental Information Disclosure

In compliance with the ongoing duty of disclosure imposed by 37 C.F.R. §1.56, Applicants submit herewith a Supplemental Information Disclosure Statement and PTO Form 1449.

Power of Attorney

Applicants include herewith an executed Power of Attorney form that revokes the previously filed Power of Attorney and appoints new representation with new Attorney Docket Number **025129.00007**. Further, Applicants have requested a Change of Correspondence, so that all communications from the USPTO be sent to the following contact and address:

**Tristan Fuierer
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In addition, pursuant to the new Power of Attorney submitted herein, the Customer Number should be changed to **24239**.

Entity Status of New Assignee

The new assignee of the subject patent application, Tiber Laboratories, qualifies as a small entity.

Amendment to the Claims

Claims 1, 5, 14-15, 20, 31, 32, 34-38, 40-43 and 53 have been amended. Claim 39 has been cancelled without prejudice. New claims 54-67 have been added. Support for the amended claims 1, 5, 14-15, 20, 31, 32, 34-38, 40-43 and 53 and newly added claims 54-64 can be found throughout the specification and claims as originally filed at, for example, at page 4, lines 6-10, page 5, line 23 through page 8, line 25, page 10, line 19 through page 12, line 5, Tables 1 and 2 found on pages 11 and 18, respectively, page 19, lines 1-10, and original claims 1, 31, 35, 39 and 53.

No new matter has been added herein.

Claim Rejections – 35 U.S.C. §112, Written Description Requirement

In the October 30, 2006 Office Action, claims 1-21, 31-48 and 53 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement for containing subject matter that was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner stated that:

“Applicant has failed to provide adequate written support for the claimed limitations directed to (1) a plurality of active ingredients (claims 1, 31, and 53), (2) plurality of dosage units (claims 1, 31 and 53), (3) combinations thereof (claims 3, 5, 32, 34-37 and 39-43), (4) at least one tablet excipient (claim 31) and (5) homogeneous suspension, granulation or composition (claims 1, 31 and 53)” (see, *e.g.*, Office Action dated October 30, 2006 at page 4, lines 13-16).

Applicants submit that claims 1-2, 4-21, 31-38, 40-48 and 53 have been amended to remove the terms “plurality of active ingredients,” “plurality of dosage units,” “combinations thereof,” “at least one tablet excipient,” and “homogeneous suspension, granulation or composition,” thus rendering the rejection moot as it pertains to these claims. Therefore, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112, first paragraph.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

1. In the October 30, 2006 Office Action, claim 3 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which Applicant regards as the invention. Specifically, the Examiner stated that:

“...it is noted that claim 3 does not explicitly refer back to the salt of said active pharmaceutical ingredient, but rather to ‘the active pharmaceutical ingredients,’ which, if interpreted in a literal manner, would actually refer back to the “active pharmaceutical ingredients” at lines 1-2 of present claim 1. In other words, the claim conceivable reads upon an embodiment wherein the composition consists essentially of the active pharmaceutical ingredients selected from the maleate, citrate, chloride, bromide, acetate and sulfate salts of phenylephrine, pyrilamine and dextromethorphan, which is clearly contradictory to the end result of the process described in present claim 1, *i.e.*, the formulation of a composition comprising the tannate salts of phenylephrine, pyrilamine and dextromethorphan” (see, *e.g.*, Office Action dated 10/30/2006 at page 9, line 17 through page 10, line 2).

Applicants respectfully submit that claim 3 has been amended to recite:

3. (Currently Amended) The composition of claim 1 wherein the salt or free base of said active pharmaceutical ingredients are selected from the group consisting of maleate, citrate, chloride, bromide, acetate and sulfate.

As amended, claim 3 now clearly refers to the types of salts or free bases of the active pharmaceutical ingredients (*i.e.* phenylephrine, pyrilamine and dextromethorphan compounds) that can be *initially* used in the method to *produce* the tannate salts (*i.e.*, the end product form of the active pharmaceutical ingredients) of the claimed composition. Applicants respectfully request that the Examiner withdraw this rejection under 35 U.S.C. §112, second paragraph.

2. In the October 30, 2006 Office Action, claims 1-21, 31-48 and 53 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner objected to the “plurality” and “homogeneous suspension” language.

As indicated herein above, claims 1, 31 and 53 have been amended to remove the “plurality” and “homogeneous suspension” language, thus rendering the rejection moot as it pertains to these claims. Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. §112, second paragraph as it pertains to these terms.

With regards to the term “without isolation or purification,” the Examiner stated:

“Furthermore, Applicant’s newly added limitation directed to “without isolation or purification” has been noted, but renders the claim indefinite because Applicant has failed to make clear whether the claim(s) intend that the tannate salts are not isolated or purified prior to combination with the at least one suspending agent or whether the combination of the tannate salts and the at least one suspending agent is not further isolated or purified after the step of combining the two components. In other words, Applicant has not clearly delineated on the record to which components the isolation or purification step refers (see, e.g., Office Action dated October 30, 2006, at page 11, lines 8-13).

Applicants submit that claim 1 has been amended to recite that the tannate salts in the second solution are combined, without isolation or purification, with the liquid pharmaceutical carrier to produce a liquid dosage form that includes the tannate salts of phenylephrine, pyrilamine and dextromethorphan and the liquid pharmaceutical carrier; claim 31 has been amended to recite that the tannate salts in the first solution are combined, without isolation and purification, with the powder mixture followed by the addition of one or more excipients; and claim 53 has been amended to recite that at least a portion of the solution which contains the tannate salts is transferred to the dispersion without isolation or purification. In light of these amendments, Applicant respectfully requests that the Examiner withdraw this rejection under 35 U.S.C. §112, second paragraph.

Claim Rejections Under 35 U.S.C. §103(a)

In the October 30, 2006 Office Action, claims 1-21, 31-48 and 53 were rejected under 35 U.S.C. §103(a) as being unpatentable over Gordziel (U.S. Patent No. 6,287,597, hereinafter “Gordziel”) in view of Venkataraman (U.S. Patent No. 6,509,492, hereinafter “Venkataraman”) and Chopdekar *et al.* (U.S. Patent No. 5,599,846, hereinafter “Chopdekar”). Specifically, the Examiner stated that:

“One of ordinary skill in the art would have found it *prima facie* obvious to combine disclosures of Gordziel and Venkataraman to compose a pharmaceutical composition of phenylephrine tannate, pyrilamine tannate and dextromethorphan tannate because Venkataraman teaches the preferable combination of an antihistamine, decongestant and antitussive (i.e. dextromethorphan tannate, see Table 1 at col. 7) as an

efficacious and comprehensive approach to treating viral infection or symptoms, cold symptoms, allergic rhinitis, runny nose, cough, post-nasal drip, rhinorrhea and sinusitis (Venkataraman, col. 8, lines 5-27). The skilled artisan would have been motivated to do so in order to provide a single composition with broader therapeutic effects and an enhanced benefit to the patient. Additionally, both the compositions of Gordziel and those of Venkataraman are each known for the same therapeutic purpose (i.e. treating the common cold, allergic rhinitis, sinusitis, etc.) and, therefore, the combination of the composition of Gordziel with that of Venkataraman would have naturally commended itself, and have been *prima facie* obvious, to the skilled artisan. Motivation to administer two compositions flows logically from the fact that each was known to be administered for the same therapeutic endpoint and it is generally obvious to use in combination two or more agents that have previously been used separately for the same purpose. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069.

Additionally, it is noted that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the process of Chopdekar *et al.* for formulation of the tannate salts of phenylephrine, pyrilamine and dextromethorphan rather than the conventional isopropanol route because the process of Chopdekar *et al.* is capable of producing (a) a much higher yield of tannate(s) and (b) a much higher level or purity of those tannate(s), as compared with the synthetic isopropanol route. Such a person would have been motivated to do so because the enhanced yield and purity would have allowed for greater uniformity in the pharmaceutical composition and would also have enhanced the therapeutic effect of the composition while minimizing exposure to degradation products and organic solvents, which may hinder the therapeutic activity of the composition.

Though the process of Chopdekar *et al.* is not necessarily the same as that presently recited in the claims in the order or step by which the process proceeds, the invention as claimed is the composition of phenylephrine tannate, pyrilamine tannate, and dextromethorphan tannate, regardless of how Applicant has claimed the composition is produced. Process limitations only become patentable distinctions if they confer upon the product a physical or structural property that is not found in the composition of the prior art (see, *e.g.*, Office Action dated October 30, 2006, at page 13, line 24 through page 15, line 5).

Applicants respectfully traverse this rejection.

In order to establish a *prima facie* case showing obviousness over the prior art, the Examiner

must show the following three elements: (1) a suggestion or motivation to combine or modify the cited references; (2) a reasonable expectation of success; and (3) that the combination or modification of the prior art references teaches all of the limitations of the claim at issue. Failure to show any one of the foregoing negates a *prima facie* showing. The initial burden is on the Examiner to provide some suggestion of the desirability of doing what the inventor has done. M.P.E.P. §2142 *et seq.*

Whether the rejection for obviousness depends on a combination of prior art references or a single reference alone, there must be some teaching, suggestion, or motivation to combine or modify the references. Usually, the suggestion comes from the teachings of the pertinent references, or from the ordinary knowledge of those skilled in the art that certain references are of special importance. It is clear that the suggestion or motivation cannot be derived from the teachings of the Applicant. Therefore, when examining the patentability of a claimed invention that combines known elements, “the question is ***whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination.***” *In re Rouffet*, 149 F.3d 1350, 1355-1356 (Fed. Cir. 1998) (emphasis added); *see also*, *GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462 (Fed. Cir. 1984); and *In re Beattie*, 974 F.2d 1309, 1311-1312 (Fed. Cir. 1992). In other words, it is not sufficient that the prior art ***could*** so be modified. Rather, the prior art must teach or suggest that the prior art ***should*** be modified. *See*, *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

The present invention generally provides for a pharmaceutical composition ***consisting of*** tannate salts of phenylephrine, pyrilamine and dextromethorphan together with either a liquid or granulate pharmaceutical carrier.

Gordziel describes the combination of pyrilamine tannate and phenylephrine tannate having sympathomimetic decongestant and antihistamine properties superior to the use of either one of the tannate compounds alone (see, *e.g.*, Gordziel at col. 2, lines 10-13). Importantly, Gordziel only discusses the combination of two sympathomimetic drugs, not the combination of sympathomimetic drugs and other, non-sympathomimetic drugs such as antitussives, expectorants, etc. According to Dorland’s Medical Dictionary, the term “sympathomimetic” is defined as “the mimicking of the effects of impulses conveyed by adrenergic postganglionic fibers of the sympathetic nervous system” (see, *e.g.*, “Dorlands Medical Dictionary,” Merck Source, 27 March 2007, < <http://www.mercksource.com/> >). The dextromethorphan compound

utilized in Applicant's invention is an antitussive agent, *not* a sympathomimetic compound. No where in Gordziel is there any suggestion, teaching, or motivation to combine compounds other than sympathomimetic compounds. As such, the present invention is not obvious in view of Gordziel.

The addition of Venkataraman does not remedy the deficiency of the Gordziel reference. Venkataraman discloses numerous combinations of antihistamines, and/or decongestants and/or antitussives and/or expectorants as an efficacious and comprehensive approach to treating viral infection or symptoms, cold symptoms, allergic rhinitis, runny nose, cough, post-nasal drip, rhinorrhea and sinusitis. Indeed, Venkataraman discloses that:

“Preferred tannate compositions comprising two or more pharmaceutical classes include an antihistamine and a decongestant; and antihistamine and an antitussive; an antihistamine and an expectorant; and antihistamine, a decongestant and an antitussive; and antihistamine, a decongestant, an antitussive and an expectorant; an antihistamine, an antitussive and an expectorant; a decongestant and an antitussive; a decongestant and an expectorant; a decongestant, an antitussive and an expectorant; an antitussive and an expectorant” (see, *e.g.*, Venkataraman at col. 7, lines 5-14).

In addition to the vast number of possible combinations disclosed, Venkataraman further discloses that tannate compositions of the present invention comprise pharmaceutical compositions including, but not limited to, the tannate compounds listed in Table 1 (see below).

TABLE 1

Therapeutic agents
<u>Antihistamines</u>
Azatadine tannate
Chlorpheniramine tannate
Brompheniramine tannate
Chlorcyclizine tannate
Dexchlorpheniramine tannate
Dexbrompheniramine tannate
Triprolidine tannate
Diphenhydramine tannate
Doxylamine tannate
Carbinoxamine tannate
Phenindamine tannate
Pyrilamine tannate

TABLE 1-continued

Therapeutic agents
Thonzylamine tannate
Tripolidine tannate
<u>Decongestants</u>
Pseudoephedrine tannate
Phenylephrine tannate
<u>Cough Suppressants/Antitussives</u>
Dextromethorphan tannate
<u>Expectorants</u>
Guaifenesin tannate

(see, *e.g.*, Venkataraman at Table 1, at col. 7 line 52 through col. 8, line 15)

It is the Examiner's position that one skilled in the art would be able to just pick the compounds of the claimed invention from the laundry list provided in the Venkataraman reference. However, conspicuously missing from the record is any substantive evidence that one of ordinary skill in the art would have been motivated to choose the presently claimed compounds to arrive at Applicants' claimed invention consisting of phenylephrine tannate, dextromethorphan tannate, pyrilamine tannate and a liquid pharmaceutical carrier or granulate mixture .

Merely identifying all of the elements of a claim or their equivalents in the prior art is not sufficient. Almost all inventions are combination of old elements, and an Examiner may often find every element of a claimed invention in the prior art. If this finding were sufficient "to negate patentability, very few patents would ever issue." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998). Therefore, in order to establish a *prima facie* rejection for obviousness, an "examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would [*not* could] select the elements from the cited prior art references for combination in the manner claimed." *In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Further, as stated by the court in *In re Kratz*, 201 U.S.P.Q. 71 (C.C.P.A.), "[e]ven if the bare lists of component found...were in the prior art, those extensive lists are quite mute in directing one having ordinary skill in the art to any particular compound for any purpose." The Court reversed

the Examiner's rejection for obviousness, and stated that for there to be a denial of patentability "the prior art itself [should] further provide some foreseeability or predictability that the compound is a significant...ingredient." Clearly, while Applicants' combination may have been disclosed in the Venkataraman among numerous other possible combinations, there is no teaching, suggestion or motivation to one skilled in the art to combine the three compounds claimed in the present invention over any of the other combinations disclosed.

Lastly, the addition of the Chopdekar reference does not remedy the deficiencies of the Venkataraman and Gordziel references. Chopdekar describes a process for the preparation of tannate forms, for example, of pyrilamine and/or phenylephrine, which may then be used to prepare compositions that includes those tannate salt forms of phenylephrine and pyrilamine. According to M.P.E.P. §2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Nowhere in Chopdekar is there any suggestion, teaching, or motivation to combine compounds other than pyrilamine and phenylephrine.

In summary, there is no motivation in any of the cited references that would cause one of ordinary skill in the art to combine the references in the manner suggested by the Examiner. Accordingly, Applicants submit that the claimed invention is patentable over the cited references, taken alone or in combination, and respectfully request reconsideration and withdrawal of the rejection.

Obviousness-Type Double Patenting

In the October 30, 2006 Office Action, the Examiner provisionally rejected claims 1-21, 31-48 and 53 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21, 31-48 and 53 of co-pending U.S. Patent Application No. 10/047,578.

When the obviousness-type double patenting rejection is the only rejection remaining to the presently pending case AND **if** the presently pending claims are an obvious variation of the

invention defined in claims 1-21, 31-48 and 53 of co-pending U.S. Patent Application No. 10/047,578 (which can only be objectively assessed when the only rejection remaining in the presently pending case is the obviousness-type double patenting rejection), Applicants will consider submitting the required terminal disclaimer.

Petition for Extension of Time/Fees Payable

Applicants hereby petition for a two (2) month extension of time, extending the deadline for responding to the October 30, 2006 Office Action from January 30, 2007 to March 30, 2007. The fee of \$225.00 specified in 37 C.F.R. §1.17(a)(1) for such two (2) month extension is hereby enclosed.

One (1) dependent claim has been cancelled and eleven (11) claims, two (2) of which are independent, have been added herein. As such, claim fees of $[(2 \times \$100.00) + (11 \times \$25.00)] - (1 \times \$25.00) = \450.00 is due.

In addition, a fee of \$395.00 for the filing of the Request for Continued Examination is due.

The total fee of \$1,070.00 is being paid by Electronic Funds Transfer. Authorization is hereby given to charge any deficiency in applicable fees for this response to Deposit Account No. 13-4365 in the name of Moore & Van Allen, PLLC.


Conclusion

Claims 1-21, 31-38, 40-48 and 53-64 are in form and condition for allowance. If any additional issues remain, the Examiner is requested to contact the undersigned attorney at (919) 286-8021 to discuss same.

Respectfully submitted,

MOORE & VAN ALLEN PLLC

Date: March 28, 2007

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